

1. A carrier for transporting a polyanionic macromolecule across a biological barrier of a cell comprising:
a biocompatible hydrophilic backbone polymer; and
two or more polycationic polymers covalently linked to the biocompatible hydrophilic backbone polymer by a linker.
2. The carrier of claim 1, wherein the biocompatible hydrophilic backbone is selected from the group consisting of polyethylene glycol (PEG), poly(N-(2-hydroxypropyl)methacrylamide), and copolymers thereof.
3. The carrier of claim 2, wherein the polycationic polymers are polyethylenimine (PEI).
4. The carrier of claim 1, wherein the polycationic polymers are selected from the group consisting of polyalkylamine (PAM), polyethylenimine (PEI), polylysine (PL), a polypeptide, chitosan, a polysaccharide, and copolymers thereof.
5. The carrier of claim 1, further comprising at least one targeting moiety connected to the biocompatible hydrophilic backbone or to one of the two or more polycationic polymers.
6. The carrier of claim 5, wherein the targeting moiety is selected from the group consisting of a ligand, an antigen, a hapten, biotin, lectin, galactose, galactosamine, a protein, a histone, a polypeptide, a lipid, a carbohydrate, a vitamin, and a combination thereof.

1 7. The carrier of claim 1, further comprising at least one lysis agent connected to the
2 biocompatible hydrophilic backbone or to one of the two or more polycationic polymers.

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4 8. The carrier of claim 7, wherein the at least one lysis agent is selected from the group
5 consisting of a viral peptide, a bacterial toxin, a lytic peptide, aleveolysin, bifermentolysin,
6 boutulinolysin, capriciolysin, cereolysin O, chauveolysin, histolyticolysin O, pneumolysin,
7 sealigerolysin, septicolysin O, sordellilysin, streptoslysin O, tenaolysin or thuringolysin O, and active
8 fragments thereof
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12 9. The carrier of claim 1, wherein the linker has a length from about 2 to about 100 atoms.

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14 10. The carrier of claim 9, wherein the linker is selected from the group consisting of a
15 hydrocarbon chain, a PEG fragment, a polypeptide, a linear polymer containing an ester bond, a
16 linear polymer containing an amide bond, a linear polymer containing a disulfide bond, a linear
17 polymer containing a hydrozone bond, and a linear polymer containing an oxime bond.

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19 11. The carrier of claim 9, wherein the length of the linker is within the range from about 3
20 atoms to about 30 atoms.

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22 12. The carrier of claim 1, wherein the biocompatible hydrophilic backbone has a molecular
23 weight in the range from about 1,000 to about 1,000,000 and the polycationic polymers have a
24 molecular weight in the range from about 100 to about 100,000.
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13. The carrier of claim 12, wherein the molecular weight of the biocompatible hydrophilic backbone is in the range from about 5,000 to about 100,000.

14. The carrier of claim 12, wherein the molecular weight of the biocompatible hydrophilic backbone is in the range from about 20,000 to about 40,000.

15. The carrier of claim 12, wherein the molecular weight of the polycationic polymers is in the range from about 200 to about 10,000.

16. The carrier of claim 12, wherein the molecular weight of the polycationic polymers is in the range from about 400 to about 2,000.

17. The carrier of claim 1, wherein the biocompatible hydrophilic backbone is polyethylene glycol and the polycationic polymers is polyethylenimine.

18. The carrier of claim 17, wherein from about 4 to about 100 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.

19. The carrier of claim 17, wherein from about 8 to about 15 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.

20. The carrier of claim 17, wherein the molecular weight of the biocompatible hydrophilic backbone is in the range from about 20,000 to about 40,000.

21. The carrier of claim 17, wherein the molecular weight of polycationic polymers is in the range from about 400 to about 2,000.

- 1 22. The carrier of claim 17, wherein the linker is selected from the group consisting of a
2 hydrocarbon chain, a PEG fragment, a polypeptide, a linear polymer containing an ester bond, a
3 linear polymer containing an amide bond, a linear polymer containing a disulfide bond, a linear
4 polymer containing a hydrozone bond, and a linear polymer containing an oxime bond.
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6 23. The carrier of claim 17, further comprising at least one targeting moiety connected to the
7 biocompatible hydrophilic backbone or to one of the two or more polycationic polymers.
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9 24. The carrier of claim 23, wherein the targeting moiety is selected from the group consisting
10 of a ligand, an antigen, a hapten, biotin, lectin, galactose, galactosamine, a protein, a histone, a
11 polypeptide, a lipid, a carbohydrate, a vitamin, and a combination thereof.
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13 25. The carrier of claim 17, further comprising at least one lysis agent connected to the
14 biocompatible hydrophilic backbone or to one of the two or more polycationic polymers.
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16 26. The carrier of claim 25, wherein the at least one lysis agent is selected from the group
17 consisting of a viral peptide, a bacterial toxin, a lytic peptide, aleveolysin, bifermentolysin,
18 boutulinolysin, capriciolysin, cereolysin O, chauveolysin, histolyticolysin O, pneumolysin,
19 sealigerolysin, septicolysin O, sordellilysin, streptosolysin O, tenaolysin or thuringolysin O, and active
20 fragments thereof.
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22 27. The carrier of claim 17, wherein the linker is a biodegradable peptide.
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28. The carrier of claim 1, wherein from about 4 to about 100 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.

29. The carrier of claim 1, wherein from about 8 to about 15 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.

30. The carrier of claim 25, wherein the biodegradable peptide is selected from the group consisting of GlyPhePheGly and GlyPheLeuGly.

31. A complex for transporting a polyanionic macromolecule across a biological barrier of a cell comprising:

a carrier molecule for delivering the polyanionic macromolecule to the cell, the carrier molecule comprising a biocompatible hydrophilic backbone polymer and two or more polycationic polymers covalently linked to the biocompatible hydrophilic backbone polymer by a linker; and

a polyanionic macromolecule complexed with the carrier molecule.

32. The complex of claim 31, wherein the polyanionic macromolecule is a nucleic acid.

33. The complex of claim 32, wherein the polycationic polymers are PEI.

34. The complex of claim 33, wherein the biocompatible hydrophilic backbone polymer is PEG.

35. The complex of claim 33, wherein the biocompatible hydrophilic backbone polymer is HPMa.

36. The complex of claim 32, wherein the nucleic acid is selected from the group consisting of genomic DNA, plasmid DNA, synthetic DNA, and RNA.

37. The complex of claim 32, wherein the nucleic acid is selected from the group consisting of an antisense oligonucleotide, ribozyme, DNAzyme, chimeric RNA/DNA oligonucleotide, phosphorothioate oligonucleotide, 2'-O-methyl oligonucleotide, DNA-PNA conjugate, DNA-morpholino-DNA conjugate, and a combination thereof.

38. The complex of claim 31, wherein the biocompatible hydrophilic backbone has a molecular weight in the range from about 1,000 to about 1,000,000 and the polycationic polymers have a molecular weight in the range from about 100 to about 100,000.

39. The complex of claim 38, wherein the molecular weight of the biocompatible hydrophilic backbone is in the range from about 20,000 to about 40,000.

40. The complex of claim 39, wherein the molecular weight of the polycationic polymers is in the range from about 400 to about 2,000.

41. The complex of claim 31, wherein the linker is selected from the group consisting of a hydrocarbon chain, a PEG fragment, a polypeptide, a linear polymer containing an ester bond, a linear polymer containing an amide bond, a linear polymer containing a disulfide bond, a linear polymer containing a hydrozone bond, and a linear polymer containing an oxime bond.

42. The complex of claim 31, wherein the biocompatible hydrophilic backbone is selected from the group consisting of polyethylene glycol (PEG), poly (N-(2-hydroxypropyl)methacrylamide), and copolymers thereof.

43. The complex of claim 42, wherein the polycationic polymers are selected from the group consisting of polyalkylamine (PAM), polyethylenimine (PEI), polylysine (PL), a polypeptide, chitosan, a polysaccharide, and copolymers thereof.

44. The complex of claim 31, further comprising at least one targeting moiety connected to the biocompatible hydrophilic backbone or to one of the two or more polycationic polymers, the at least one targeting moiety selected from the group consisting of a ligand, an antigen, a hapten, biotin, lectin, galactose, galactosamine, a protein, a histone, a polypeptide, a lipid, a carbohydrate, and a combination thereof.

45. The complex of claim 31, further comprising at least one lysis agent connected to the biocompatible hydrophilic backbone or to one of the two or more polycationic polymers, the at least one lysis agent selected from the group consisting of a viral peptide, a bacterial toxin, a lytic peptide, aleveolysin, bifermentolysin, boutulinolysin, capriciolysin, cereolysin O, chauveolysin, histolyticolysin O, pneumolysin, sealigerolysin, septicolysin O, sordellilysin, streptosolysin O, tenaolysin or thuringolysin O, and active fragments thereof.

46. The complex of claim 31, wherein from about 4 to about 100 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.

47. The complex of claim 31, wherein from about 8 to about 15 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.

1 48. A method of transporting a polyanionic macromolecule across a biological barrier of a cell
2 comprising:

3 complexing the polyanionic macromolecule to a carrier molecule to create a complex, the
4 carrier molecule comprising a biocompatible hydrophilic backbone polymer and two or more
5 polycationic polymer covalently linked to the biocompatible hydrophilic backbone polymer by a
6 linker; and

7 contacting the cell with the complex.
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9 49. The method of claim 48, wherein the biocompatible hydrophilic backbone is selected from
10 the group consisting of polyethylene glycol (PEG), poly (N-(2-hydroxypropyl)methacrylamide),
11 and copolymers thereof.
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13 50. The method of claim 49, wherein the polycationic polymers are selected from the group
14 consisting of polyalkylamine (PAM), polyethylenimine (PEI), polylysine (PL), a polypeptide,
15 chitosan, a polysaccharide, and copolymers thereof.
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17 51. The method of claim 48, further comprising at least one targeting moiety connected to the
18 biocompatible hydrophilic backbone or to one of the two or more polycationic polymers, the
19 targeting moiety selected from the group consisting of a ligand, an antigen, a hapten, biotin, lectin,
20 galactose, galactosamine, a protein, a histone, a polypeptide, a lipid, a carbohydrate, and a
21 combination thereof.
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1 52. The method of claim 48, further comprising at least one lysis agent connected to the
2 biocompatible hydrophilic backbone or to one of the two or more polycationic polymers, the at
3 least one lysis agent selected from the group consisting of a viral peptide, a bacterial toxin, a lytic
4 peptide, aleveolysin, bifermentolysin, boutulinolysin, capriciolysin, cereolysin O, chauveolysin,
5 histolyticolysin O, pneumolysin, sealigerolysin, septicolysin O, sordellilysin, streptoslysin O,
6 tenaolysin or thuringolysin O, and active fragments thereof.
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10 53. The method of claim 48, wherein the linker has a length from about 2 to about 100 atoms.
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12 54. The method of claim 53, wherein the linker is selected from the group consisting of a
13 hydrocarbon chain, a PEG fragment, a polypeptide, a linear polymer containing an ester bond, a
14 linear polymer containing an amide bond, a linear polymer containing a disulfide bond, a linear
15 polymer containing a hydrozone bond, and a linear polymer containing an oxime bond.
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17 55. The method of claim 53, wherein the linker is a biodegradable peptide.
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19 56. The method of claim 55, wherein the biodegradable peptide is selected from the group
20 consisting of GlyPhePheGly and GlyPheLeuGly.
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22 57. The method of claim 48, wherein the biocompatible hydrophilic backbone has a molecular
23 weight in the range from about 1,000 to about 1,000,000 and the polycationic polymers have a
24 molecular weight in the range from about 100 to about 100,000.
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58. The method of claim 57, wherein the molecular weight of the biocompatible hydrophilic backbone is in the range from about 20,000 to about 40,000.

59. The method of claim 57, wherein the molecular weight of the polycationic polymers is in the range from about 400 to about 2,000.

60. The method of claim 57, wherein the biocompatible hydrophilic backbone is polyethylene glycol and the polycationic polymers are polyethylenimine.

61. The method of claim 60, wherein the molecular weight of the biocompatible hydrophilic backbone is in the range from about 20,000 to about 40,000.

62. The method of claim 60, wherein the molecular weight of the polycationic polymers is in the range from about 400 to about 2,000.

63. The method of claim 48, wherein from about 4 to about 100 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.

64. The method of claim 48, wherein from about 8 to about 15 polycationic polymers are covalently linked to the biocompatible hydrophilic backbone polymer by a linker.